In the Specification

Please substitute the following paragraph on page 9, beginning at line 19 through to page 10, line 22:

In an eighth aspect, the invention provides a polypeptide of the first aspect of the invention, or a nucleic acid molecule of the second or third aspect of the invention, or a vector of the fourth aspect of the invention, or a ligand of the sixth aspect of the invention, or a compound of the seventh aspect of the invention, for use in therapy or diagnosis of a disease in which human growth hormone is implicated. Such diseases and disorders may include reproductive disorders, ~~pregananey~~ pregnancy disorder, such as gestational trophoblastic disease, developmental disorders such as Silver-Russell syndrome, growth disorders, growth hormone deficiency, Cushing's disease, endocrine disorders, cell proliferative disorders, including neoplasm, carcinoma, pituitary tumour, ovary tumour, melanoma, lung, colorectal, breast, pancreas, head and neck, placental site trophoblastic tumor, adenocarcinoma, choriocarcinoma, osteosarcoma and other solid tumours; angiogeneisis, myeloproliferative disorders; autoimmune/inflammatory disorders; cardiovascular disorders; neurological disorders, pain; metabolic disorders including diabetes mellitus, osteoporosis, and obesity, cachexia, AIDS, renal disease; lung injury; ageing; infections including viral infection, bacterial infection, fungal infection and parasitic infection, and other pathological conditions. Preferably, the disease is one in which endocrine function, particularly growth hormones are implicated (see, for example, Arato G., Fulop V., Degrell P., Szigetvari I. Pathol. Oncol. Res. 2000 6(4):292-4; Hitchins M.P., Stanier P., Preece M.A. and Moore GE., J. Med. Genet. 2001 Dec 38(12):810-9; Rhoton-Vlasak A., Wagner J.M., Rutgers J.L., Baergen R.N., Young R.H., Roche P.C., Plummer T.B. and Gleich G.J., Hum Pathol 1998 Mar 29(3):280-8; Llovera M., Pichard C., Bernichtein S., Jeay S., Touraine P., Kelly P.A. and Goffin V., Oncogene, 2000 Sep 28 19(41):4695-705; Savage M.O., Scommegna S., Carroll P.V., Ho J.T., Monson J.P., Besser G.M. and Grossman AB., Horm. Res. 2002 58 Suppl 1:39-43; Aimaretti G., Corneli G., Bellone S., Baffoni C., Camanni F. and Ghigo E., J. Pediatr. Endocrinol. Metab. 2001 14 Suppl 5:1233-42; Berger P., Untergasser G., Hermann M., Hittmair A., Madersbacher S. and Dirnhofer S., Hum. Pathol. 1999 Oct 30(10):1201-6; Hamilton J., Chitayat D., Blaser S., Cohen L.E., Phillips J.A. 3rd and Daneman D., Am. J. Med. Genet. 1998 Nov 2 80(2):128-32; Gonzalez-

Rodriguez E., Jaramillo-Rangel G. and Barrera-Saldana H.A., Am. J. Med. Genet. 1997 Nov 12 72(4):399-402; Perez Jurado L.A., Argente J., Barrios V., Pozo J., Munoz M.T., Hernandez M. and Francke U., J. Pediatr. Endocrinol. Metab. 1997 Mar-Apr 10(2):185-90; Saeger W. and Lubke D., Endocr. Pathol. 1996 Spring 7(1):21-35; Conzemius M.G., Graham J.C., Haynes J.S. and Graham C.A., Am. J. Vet. Res. 2000 Jun 61(6):646-50; Bartlett D.L., Charland S., Torosian M.H., Cancer 1994 Mar 1 73(5):1499-504). These molecules may also be used in the manufacture of a medicament for the treatment of such disorders.

Please substitute the following paragraph on page 15, beginning at line 32 through to page 16, line 10:

The functionally-equivalent polypeptides of the first aspect of the invention may also be polypeptides which have been identified using one or more techniques of structural alignment. For example, the Inpharmatica ~~Genome Threader~~™ GENOME THREADER technology that forms one aspect of the search tools used to generate the Biopendium search database may be used (see co-pending International Patent Application No. PCT/GB01/01105) to identify polypeptides of presently-unknown function which, while having low sequence identity as compared to the INSP105 polypeptide, are predicted to be growth hormone proteins, said method utilising a polypeptide of the first aspect of the invention, by virtue of sharing significant struetural homology with the INSP105 polypeptide sequenees. By "significant structural homology" is meant that the Inpharmatica Genome Threader™ predicts two proteins to share structural homology with a certainty of at least 10% and above.

Please substitute the following paragraph on page 23, beginning at line 31 through to page 24, line 19:

In many cases, isolated cDNA sequences will be incomplete, in that the region encoding the polypeptide will be cut short, normally at the 5' end. Several methods are available to obtain full length cDNAs, or to extend short cDNAs. Such sequences may be extended utilising a partial nucleotide sequence and employing various methods known in the art to detect upstream sequences such as promoters and regulatory elements. For example, one method which may be employed is

based on the method of Rapid Amplification of cDNA Ends (RACE; see, for example, Frohman *et al.*, PNAS USA 85, 8998-9002, 1988). Recent modifications of this technique, exemplified by the ~~Marathon~~™ MARATHON technology (Clontech Laboratories Inc.), for example, have significantly simplified the search for longer cDNAs. A slightly different technique, termed "restriction-site" PCR, uses universal primers to retrieve unknown nucleic acid sequence adjacent a known locus (Sarkar, G. (1993) PCR Methods Applic. 2:318-322). Inverse PCR may also be used to amplify or to extend sequences using divergent primers based on a known region (Triglia, T. *et al.* (1988) Nucleic Acids Res. 16:8186). Another method which may be used is capture PCR which involves PCR amplification of DNA fragments adjacent a known sequence in human and yeast artificial chromosome DNA (Lagerstrom, M. *et al.* (1991) PCR Methods Applic., 1, 111-119). Another method which may be used to retrieve unknown sequences is that of Parker, J.D. *et al.* (1991); Nucleic Acids Res. 19:3055-3060). Additionally, one may use PCR, nested primers, and ~~PromoterFinder~~™ PROMOTERFINDER libraries to walk genomic DNA (Clontech, Palo Alto, CA). This process avoids the need to screen libraries and is useful in finding intron/exon junctions.

Please substitute the following paragraph on page 27, beginning at line 19 through to page 28, line 6:

In addition to control sequences, it may be desirable to add regulatory sequences that allow for regulation of the expression of the polypeptide relative to the growth of the host cell. Examples of regulatory sequences are those which cause the expression of a gene to be increased or decreased in response to a chemical or physical stimulus, including the presence of a regulatory compound or to various temperature or metabolic conditions. Regulatory sequences are those non-translated regions of the vector, such as enhancers, promoters and 5' and 3' untranslated regions. These interact with host cellular proteins to carry out transcription and translation. Such regulatory sequences may vary in their strength and specificity. Depending on the vector system and host utilised, any number of suitable transcription and translation elements, including constitutive and inducible promoters, may be used. For example, when cloning in bacterial systems, inducible promoters such as the hybrid lacZ promoter of the Bluescript phagemid (Stratagene, LaJolla, CA) or ~~pSport1~~™ PSPORT1 plasmid (Gibco BRL) and the like may be used. The baculovirus polyhedrin promoter may be used in insect cells. Promoters or enhancers derived from the genomes of plant cells (for example, heat shock,

RUBISCO and storage protein genes) or from plant viruses (for example, viral promoters or leader sequences) may be cloned into the vector. In mammalian cell systems, promoters from mammalian genes or from mammalian viruses are preferable. If it is necessary to generate a cell line that contains multiple copies of the sequence, vectors based on SV40 or EBV may be used with an appropriate selectable marker.

Please substitute the following paragraph on page 47, beginning at line 16:

Such kits will be of use in diagnosing a disease or disorder or susceptibility to disease or disorder in which endocrine proteins are implicated. Such diseases and disorders may include reproductive disorders, ~~pregananey~~ pregnancy disorder, such as gestational trophoblastic disease, developmental disorders such as Silver-Russell syndrome, growth disorders, growth hormone deficiency, Cushing's disease, endocrine disorders, cell proliferative disorders, including neoplasm, carcinoma, pituitary tumour, ovary tumour, melanoma, lung, colorectal, breast, pancreas, head and neck, placental site trophoblastic tumor, adenocarcinoma, choriocarcinoma, osteosarcoma and other solid tumours; angiogeneisis, myeloproliferative disorders; autoimmune/inflammatory disorders; cardiovascular disorders; neurological disorders, pain; metabolic disorders including diabetes mellitus, osteoporosis, and obesity, cachexia, AIDS, renal disease; lung injury; ageing; infections including viral infection, bacterial infection, fungal infection and parasitic infection, and other pathological conditions. Preferably, the disease is one in which endocrine function, particularly growth hormones are implicated.

Please substitute the following paragraph on page 48, beginning at line 5:

Figure 1 shows an alignment of full length INSP105 ~~(SEQ ID NO:6)~~ (SEQ ID NO:8, identified as "Query") versus P01242 (SEQ ID NO:30, identified as "Sbjct"), placental growth hormone (GH-V) from *H. sapiens*. The A-B loop is marked by asterisks.

Please substitute the following paragraph on page 48, beginning at line 9:

Figure 3: Predicted nucleotide sequence of INSP105 with translation (SEQ ID NO:31)

Please substitute the following paragraphs on page 48, beginning at line 12:

Figure 5: Alignment of INSP105 (SEQ ID NO:31) with pENTR clone–miniprep 6 (SEQ ID NO:32) indicating the position of PCR primers used to re-amplify the correct 5' end of the cDNA

Figure 6: Alignment of INSP105 (SEQ ID NO:31) with pENTR clone–miniprep 10 (SEQ ID NO:33) indicating the position of PCR primers used to re-amplify the correct central region of the cDNA

Figure 7: Alignment of INSP105 (SEQ ID NO:31) with pENTR clone–miniprep 3 (SEQ ID NO:34) indicating the position of PCR primers used to re-amplify the correct 3' end of the cDNA

Figure 8: Nucleotide sequence and translation of cloned INSP105 ORF (SEQ ID NO:35)

Please substitute the following paragraph on page 49, beginning at line 22 through to page 50, line 2:

PCR primers were designed to amplify exons 1 (partial), 2, 3, 4 and 5 of INSP105 (Table 1, Figures 3 and 4). The forward primer for exon 2 (INSP105-exon2F) contains the partial sequence of the Gateway attB1 site (5' GCAGGCTTC (SEQ ID NO:36)), a Kozak sequence (5' GCCACC (SEQ ID NO:37)) and 10 bases of exon 1. The reverse primer for exon 2 (INSP105-exon2R) has an overlap of 20 bases with exon 3 of INSP105 at its 5' end. The forward primer for exon 3 (INSP105–exon3F) has a 16bp overlap with exon 2 of INSP105 at its 5' end. The reverse primer for exon 3 (INSP105–exon3R has an overlap of 16 bases with exon 4 of INSP105 at its 5' end). The forward primer for exon 4 (INSP105–exon4F) has a 16bp overlap with exon 3 of INSP105 at its 5' end. The reverse primer for exon 4 (INSP105–exon4R has an overlap of 16 bases with exon 5 of INSP105 at its 5' end). The forward primer for exon 5 (INSP105–exon5F) has a 16 bp overlap with exon 4 of INSP105 at its 5' end. The reverse primer for exon 5 (INSP105–exon5R) contains a 5HIS sequence at the 5' end.

Please substitute the following paragraph on page 51, beginning at line 22, through to page 52, line 10:

The INSP105 ORF was subcloned into pDONR221 using the ~~Gateway~~™ GATEWAY cloning system (Invitrogen). Gateway-modified INSP105 ORF was transferred to pDONR221 using BP clonase as follows: 5µl of Gateway-modified INSP105 ORF was incubated with 1.5µl pDONR221 (0.1µg/µl), 2µl BP buffer and 1.5µl of BP clonase enzyme mix (Invitrogen) at RT for 1h. The reaction was stopped by addition of 1µl proteinase K (2µg) and incubated at 37°C for a further 10 min. An aliquot of this reaction (1µl) was used to transform 20µl of *E. coli* DH10B cells (Invitrogen) (diluted 1/5 in sterile water) by electroporation using a Biorad Gene Pulser according to the manufacturer's recommendations. Electroporated cells were transferred to 12ml polypropylene tubes, diluted by addition of 1000µl of LB medium and incubated for 1h at 37°C with shaking. Transformants (50µl) were plated on LB plates containing 40µg/ml of kanamycin and incubated over night at 37°C with shaking. Mini prep DNA was prepared from 12 of the resultant colonies using a Qiaprep Turbo 9600 robotic system (Qiagen). Mini-prep DNA was eluted in 100µl of elution buffer. Plasmid mini prep DNA (200-500ng) was then subjected to DNA sequencing with M13F and M13R sequencing primers using the BigDyeTerminator system (Applied Biosystems cat. no. 4390246) according to the manufacturer's instructions. Sequencing reactions were purified using Dye-Ex columns (Qiagen) or Montage SEQ 96 cleanup plates (Millipore cat. no. LSKS09624) then analyzed on an Applied Biosystems 3700 sequencer. No resulting pENTR clone had the correct full length sequence. Therefore 3 pENTR clones miniprep DNA that had partially correct sequences were then used as templates to generate the full length sequence of INSP105 as follows:

Please substitute the following paragraph on page 54, beginning at line 5:

The INSP105 ORF was subcloned into pDONR221 using the ~~Gateway~~™ GATEWAY cloning system (Invitrogen). Gateway-modified INSP105 ORF was transferred to pDONR221 using BP clonase as described in section 3 above. Mini prep DNA was prepared from 6 of the resultant colonies using a Qiaprep Turbo 9600 robotic system (Qiagen). Mini-prep DNA was eluted in 100µl of elution buffer. Plasmid mini prep DNA (200-500ng) was then subjected to DNA sequencing with

M13F and M13R sequencing primers using the BigDyeTerminator system (Applied Biosystems cat. no. 4390246) according to the manufacturer's instructions. Sequencing reactions were purified using Dye-Ex columns (Qiagen) or Montage SEQ 96 cleanup plates (Millipore cat. no. LSKS09624) then analyzed on an Applied Biosystems 3700 sequencer.

Please substitute the following Table 1 on page 55:

Table 1: Primers for INSP105 cloning and sequencing

Primer	Sequence (5'-3')
GCP Forward	G GGG ACA AGT TTG TAC AAA AAA GCA GGC TTC GCC ACC (SEQ ID NO:11)
GCP Reverse	GGG GAC CAC TTT GTA CAA GAA AGC TGG GTT **TCA** *ATG GTG ATG GTG ATG GTG* (SEQ ID NO:12)
INSP105-exon2F	GCA GGC TTC GCC ACC ATG GCT GCA GGC TCC GGG ACG TCC CTG CTC CTG (SEQ ID NO:13)
INSP105-exon2R	GGA AGG TGT TGG AAT AGA CTC CAT TAC CCA AGA GCT TA (SEQ ID NO:14)
INSP105- exon3F	AGC TCT TGG GTA ATG GAG TCT ATT CCA ACA CCT TCC (SEQ ID NO:15)
INSP105- exon3R	GGA GCA GCT CTA GGT TAG ATT TCT GCT GCG TTT TCA (SEQ ID NO:16)
INSP105- exon4F	AAC GCA GCA GAA ATC TAA CCT AGA GCT GCT CCG CAT C (SEQ ID NO:17)
INSP105- exon4R	TGC CAT CTT CCA GCC TCC ACA TCA GCG TTT GGA TGC (SEQ ID NO:18)
INSP105- exon5F	CCA AAC GCT GAT GTG GAG GCT GGA AGA TGG CAG CCC (SEQ ID NO:19)
INSP105- exon5R	*GTG ATG GTG ATG GTG* GAA GCC ACA GCT GCC CTC CA (SEQ ID NO:20)
INSP105-5' end-R	GGT TAG ATT TCT GCT GCG TTT TCA CCC TGT TG (SEQ ID NO:21)
INSP105-center-F	CAA CAG GGT GAA AAC GCA GCA GAA ATC TAA CC (SEQ ID NO:22)
INSP105-center-R	GGC TGC CAT CTT CCA GCC TCC A (SEQ ID NO:23)
INSP105-3' end-F	GCA TCC AAA CGC TGA TGT GGA G (SEQ ID NO:24)
pEAK12-F	GCC AGC TTG GCA CTT GAT GT (SEQ ID NO:25)
pEAK12-R	GAT GGA GGT GGA CGT GTC AG (SEQ ID NO:26)
M13F	CAG GAA ACA GCT ATG ACC (SEQ ID NO:27)
M13R	TGT AAA ACG ACG GCC AGT (SEQ ID NO:28)

Underlined sequence = Kozak sequence
Bold = Stop codon
Italic sequence = His tag
Shaded Sequence = overlap with adjacent exon

Please insert the accompanying Sequence Listing as new pages 1-14 in the subject specification.